REMARKS

Introductory Comments:

Claims 1-22 were examined in the Office Action under reply and stand variously rejected under (1) 35 U.S.C. §102(e) (claims 1, 2, 5, 6, 9, 12-15, 17, 19 and 20); (2) 35 U.S.C. §112, second paragraph (claims 1-13); and (3) 35 U.S.C. §112, first paragraph (claims 1-22). These rejections are respectfully traversed as discussed more fully below.

The Office states that the formal drawings previously submitted fail to comply with 37 CFR §1.84. Applicants are submitting substitute formal drawings under separate cover on even date herewith.

Overview of the Above Amendments:

The specification has been amended as requested by the Office to delete the first sequence listing submitted and the hyperlink referenced at page 15.

Claims 1, 12, and 13 have been amended to recite that the Intron A fragment "has an internal deletion of at least 10 nucleotides" of the full-length Intron A sequence. Additionally, claims 1-8, 12 and 13 have been amended to recite that the expression construct "directs the transcription of a coding sequence present in the construct."

Support for these amendments can be found throughout the specification at, e.g., page 11, lines 3-6; page 11, lines 18-20; page 13, lines 23-22; page 16, lines 20-21; and page 18, lines 4-5. The foregoing amendments are made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing the unamended claims.

Rejection Under 35 U.S.C. §102(e):

Claims 1, 2, 5, 6, 9, 12-15, 17, 19 and 20 were rejected under 35 U.S.C. §102(e) as anticipated by Chapman et al., *Nucleic Acids Res.* (1991) 19:3979-3986 ("Chapman"). The Office contends the intron shown in Figure 3D of Chapman "lacks the full-length sequence of

hCMV intron A as it contains a mutation in the NF1 binding site." Office Action, page 3. However, applicants submit that Chapman fails to anticipate the claimed invention.

As an initial matter, the foregoing rejection is improper as 35 U.S.C. §102(e) pertains to "a patent granted on an application for patent by another...." Because Chapman is a literature reference and not a patent, 35 U.S.C. §102(e) does not apply. Applicants will nevertheless address the rejection under the assumption that the Examiner intended to apply Chapman under 35 U.S.C. §102(b).

The law is clear that in order to anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged as in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983). Finally, the law requires identity between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clar Corp.* 713 F.2d 760, 771, 218 USPQ 2d 781, 789 (Fed. Cir. 1983, cert. denied, 465 U.S. 1026 (1984)).

Chapman does not describe an Intron A fragment that has an internal deletion of at least 10 nucleotides of the full-length sequence as claimed. Rather, Chapman describes the cloning and sequencing of the CMV IE1 gene, and construction of mammalian cell expression plasmids using intact Intron A sequences. One of these Intron A sequences included a substitution of three base pairs to produce an NF1 consensus sequence incapable of binding NF1. See, page 3980, column 1, first full paragraph of Chapman. Accordingly, Chapman does not anticipate claims 1, 2, 5, 6, 9, 12-15, 17, 19 and 20 and this basis for rejection should be withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph:

Claims 1-13 were rejected under 35 U.S.C. §112, second paragraph as indefinite. The Office asserts: "Specific coding sequences within the expression construct can be expressed but not the expression construct itself." Additionally, the Office requests clarification regarding whether protein or RNA is measured to determine expression levels. As explained above, the claims have been amended to recite that the expression construct "directs the transcription of a coding sequence present in the construct at levels greater than those levels achieved by a corresponding construct that completely lacks an Intron A sequence." Thus, the claims are clear that enhanced expression refers to expression of a protein and not the expression construct. Thus, this basis for rejection has been overcome and withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph:

Claims 1-22 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office contends:

> The invention claims as an essential element that the intron A fragment drive expression levels to two-fold, ten-fold or fifty-fold that of a control construct without the intron A fragment. It is disclosed that a construct containing the intron A fragment from 1-51 and 741-834 increases expression by two-fold over a 'parent' vector in *in vitro* assays (figure 5) and less than two-fold in *in vivo* assays (figure 7). However, there is no actual reduction to practice or clear depiction of what structures or properties are required for generation of an intron A fragment or a fragment with 75% identity to the sequences found at positions 1-25 or 1-51 and 775-820 or 741-820 of SEQ ID NO:1 that can drive expression levels to two-fold, ten-fold or fifty-fold compared to a control without intron A.

Office Action, page 5. However, applicants submit that the application as filed indeed complies with the written description requirement of 35 U.S.C. §112, first paragraph.

In order to comply with the written description requirement, the specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). Determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981). Based on these tenets, applicants submit that they have indeed complied with the written description requirement of 35 U.S.C. §112, first paragraph.

As an initial matter, applicants note that several of the claims subject to the present rejection do not include the limitation of two-fold, ten-fold or fifty-fold. Specifically, this recitation is absent from claims 1, 5 and 9-22 and reading such a limitation into these claims is wholly improper. It is axiomatic that "a positive limitation from the specification cannot be read into a claim that does not impose that limitation" (MPEP §2106). As explained *In re Prater*, 415 F.2d 1393, 1404-05 (CCPA 1969), "reading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is a quite different thing from "reading limitations of the specification into a claim," to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim." The court found it impermissible to import subject matter from the specification into the claims. In the present case, in making the rejection, the Examiner is impermissibly importing a limitation into claims 1, 5 and 9-22 where such a limitation is not present.

In fact, claims 1, 5 and 9-22 only require that a protein encoded by the coding sequence in a construct containing the Intron A fragment is expressed at levels greater than levels achieved by a corresponding construct that completely lacks an Intron A sequence. There is no requirement for expression at levels two-fold, ten-fold or fifty-fold greater in claims 1, 5 and 9-22. Thus, the rejection under 35 U.S.C. §112, first paragraph as it relates to these claims should be withdrawn.

With respect to claims 2-4 and 6-7, applicants submit that, contrary to the Office's assertions, they have indeed exemplified an adequate number of species to support the claims. The Office asserts applicants have only shown a single construct that increases expression by two-fold over a parent vector in *in vitro* assays. Presumably, the Office is referring to the experiment detailed in Example 2. This example actually describes results of experiments done using 13 different constructs with varying Intron A deletions! See, Table 1 of the application. All but two of the 13 constructs exhibited expression levels **higher** than achieved with the parent construct. See, Figure 4 of the application. Moreover, the comparison was made to a parent vector that **retained** the full-length Intron A sequence. See, page 36, lines 3-7. Presumably, expression levels would have been much higher had the 13 different constructs been compared to expression levels from a vector that completely lacked the Intron A sequence. As explained in Chapman, cited by the Office in the art rejection, gp120 was expressed more than 100-fold better using the CMV enhancer/promoter region plus the Intron A sequence as compared with a construct that lacked this regulatory region. See, e.g., Chapman, page 3984, second full paragraph. Thus, there would be every expectation that levels of greater than two-fold, ten-fold and even fifty-fold would be achieved using constructs as claimed.

The Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> The description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional

> characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics.
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> A "representative number of species" means that the species that are adequately described are representative of the entire genus. ... What constitutes a "representative number" is an inverse function of the skill and knowledge of the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. ... Description of a representative number of species does not require the description be of such specificity that it would provide individual support for each species that the genus embraces. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) every sequence falling within the scope of the claims in order to adequately describe the Intron A fragment as claimed. Rather, the test is whether the specification contains sufficient disclosure regarding structural and functional characteristics of the claimed sequences to satisfy the written description requirement. In the pending case, the specification as filed more than adequately describes and details structure and function of the claimed polynucleotides.

Not only have applicants described multiple species falling within the generic claims, applicants have provided a starting structure, i.e., the sequences described in Figures 1-3 and Table 1, and provided functional characteristics, i.e., increased expression, coupled with known as well as a disclosed correlation between structure and function. Chapman teaches that plasmids including the Intron A sequence significantly out-perform plasmids that do not. Applicants have further taught that a variety of plasmids including various deletions of the Intron A sequence provide for enhanced expression levels. Finally, throughout the specification applicants teach the regions of the Intron A sequence contemplated for deletion or change. See, e.g., page 8, line 18 through page 9, line 14, pages 9-10, bridging paragraph; page 17, line 6 through page 18, line 13; pages 19-10, bridging paragraph.

In view of the disclosure in the specification and state of the art, it would have been plain to the skilled artisan that applicants were in possession of the claimed invention at the time the

application was filed. Accordingly, withdrawal of this basis for rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims define a patentable invention. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further written communications in this application to:

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